

## **REMARKS/ARGUMENTS**

### **1. Claim Amendments.**

Claim 1 has been amended to incorporate the elements of canceled claims 3 and 6. The molecular weight limitation on the contrast agent (7,000 Da) is taken from page 7, lines 11-14 of the specification. The molecular weight limitation on the vector (V) is taken from page 8, lines 5 to 8 of the specification. The optical reporter (R) being a cyanine dye is taken from page 12 lines 10-14 of the specification. The contrast agent is also required to be fluorescent. Claim basis can be found on page 11, lines 24-25 of the specification. Since clear basis has been shown, the amendments are not believed to add new subject matter. Further, in order to expedite prosecution, claims 2-4 and 6-7 have now been canceled. Accordingly, claims 1, 8, and 11 remain pending in the current action.

### **2. Claim Rejections: 35 USC §112.**

Previous claims 1-4, 6-8 and 11 stand rejected in this regard.

Applicants point out that the Examiner has acknowledged elsewhere in the office action, that suitable vectors (V) were already known – eg. from Smith and Penate. At the priority date of the present invention, the person skilled in the art can thus be assumed to be already aware of suitable targeting molecules (i.e. vectors) for the biological targets of current claim 1. In such circumstances, the present specification does not need to provide a comprehensive list of such vectors, since they were already within the common general knowledge of the person skilled in the art. The Examiner also acknowledges that the present specification provides additional teaching on that aspect. Applicants contend that the present specification therefore

fulfils the 35 USC §112 requirement in that regard. Applicants further point out that present claim 1 has additional limitations on the nature and molecular weight of the vector. Those, together with the specified “abnormally expressed biological target” provide clear information on how to reproduce the claimed invention. Applicants furthermore point out that present claim 1 is limited to cyanine dyes, and the present specification provides ample information and Examples on the vector labeling and use of such dyes.

Applicants contend that the present claims fulfill the 35 USC §112 requirements, and that the objection should be withdrawn.

**3. Novelty: 35 USC § 102.**

Previous claims 1-4, 6-8 and 11 stand rejected as lacking novelty over Smith (US 2004/0053823).

The objection is now relevant to claims 1, 4, 8 and 11 only. Applicants point out that Smith does not specifically describe contrast agents having a cyanine dye conjugated thereto. Applicants point out that Smith, at [0088], mentions ‘fluorescent agent’ – but does not mention specific dyes or absorption wavelength ranges. Since Smith does not disclose all the essential features of revised claim 1, that claim is believed novel over Smith. Claims 4, 8 and 11 all depend on claim 1 and are hence, by definition, also believed novel over Smith.

**4. Inventive Step: 35 USC § 103.**

Previous claims 1-4, 6-8 and 11 stand rejected as lacking an inventive step over the combination Klaveness (US 2003/0170173) and Penate [Cancer Res., vol. 61, 3978-3985 (2001)].

Applicants point out that Klaveness, at [0107] – [0110], teaches that the “optical imaging contrast substrate” described therein is required to change its properties as the result of enzyme action. That is consistent with claim 1 and Klaveness throughout, including eg. [0002], Figure 1 and Figure 2 therein. The optical contrast agents of the present invention do not have that essential feature. Hence, even if the person skilled in the art were considered to be motivated to adapt Example 25 of Klaveness, that would inevitably lead towards optical agents having properties which change under enzyme action as required by Klaveness. That feature is taught by Klaveness throughout to be essential, and hence cannot be ignored. The present claims are therefore believed inventive over Klaveness, and the inventive step rejection should be withdrawn.

Although Smith was cited for novelty purposes, applicants feel it appropriate to comment on Smith in the context of inventive step. As noted above, Smith does not specifically disclose optical reporters which are cyanine dyes. In addition, at [0088] and [0089], Smith teaches towards NIRF imaging probes, where NIRF = near-infrared fluorescence imaging. Smith makes it clear at [0088] that such NIRF probes are designed to be initially quenched, i.e. comprise a non-fluorescent fluorophore, which is subsequently activated by enzyme action to become fluorescent. Claim 1 of the present invention requires the optical imaging agents to be fluorescent, which is a very different approach. Applicants therefore contend that, even if

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the person skilled in the art was assumed to be motivated to modify Smith, any such optical imaging agents would be based on what Smith itself teaches to be a preferred design. That would mean that such probes would therefore be NIRF in nature and hence outside the scope of the present claims. The present claims are therefore also believed to be inventive over Smith.

**5. Obviousness-type Double Patenting Rejection.**

Previous claims 1-4, 6-8 and 11 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims of copending Application No(s). 10/573,604, 10/573/606, 10/582,679, 10/582,842, and 10/582,893. In response, Applicants submit that a terminal disclaimer will be filed once the instant application is indicated as allowable.

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### **CONCLUSION**

Applicants respectfully hold that the claims submitted herewith fulfill the requirements of a patentable invention and that all rejections and objections be withdrawn and claims 1, 8, and 11 be allowed.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,

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